Bovine Spongiform Encephalopathy (BSE) Feed Ban

To prevent the establishment and amplification of Bovine Spongiform Encephalopathy (BSE) through animal feed in the United States, FDA implemented a final rule that prohibits the use of most mammalian protein in feeds for ruminant animals. This rule, 21 CFR Part 589.2000 Code of Federal Regulations, became effective on August 4, 1997 (here called the BSE/Ruminant Feed regulation.) Inspections of renderers, feed mills, ruminant feeders, protein blenders, pet food manufacturers, pet food salvagers, animal feed distributors and transporters, ruminant feeders, and others have been conducted to determine compliance with the BSE/Ruminant Feed regulations.

Warning Letter Issued for BSE Feed Ban Violations

On May 19, 2004, FDA's New Jersey District Office issued a Warning Letter to Randall Copeland, Executive Vice-president of Operations, Menu Foods, Inc., Pennsauken, New Jersey. FDA conducted an inspection of this animal feed manufacturing operation on February 2 - 3, 2004.

This inspection revealed a significant deviation from the requirements set forth in Title 21, Code of Federal Regulations, Part 589.2000 (21 CFR 589.2000) - Animal proteins prohibited in ruminant feed. The regulation is intended to prevent the establishment and amplification of Bovine Spongiform Encephalopathy (BSE). During this inspection our investigators determined that the firm manufactured a canned animal food containing protein sources of bovine origin including beef lung. However, the lot failed to bear the cautionary statement "Do not feed to cattle or other ruminants," as required by 21 CFR 589.2000.

FDA further suggested in the Warning Letter that this statement be distinguished by different type size or color, or other means of highlighting so that the statement is readily noticed by the purchaser. The firm introduced this product without the required cautionary statement into interstate commerce on October 22, 2003.

Warning Letter Issued to Ranch Owner for Feeding Prohibited Material to Ruminants

On June 10, 2004, FDA's Dallas District Office issued a Warning Letter to Jack Chapman, Owner of Chapman Ranch, Lampasas, Texas. An FDA inspection of this ruminant feeding operation was conducted on February 26 - March 1, 2004. The inspection found significant deviations from the requirements set forth in 21 CFR 589.2000. This regulation is intended to prevent the establishment and amplification of BSE.

FDA's inspection revealed that Mr. Chapman fed prohibited material, as defined by 21 CFR 589.2000(a), to ruminants. This prohibited material consisted of manufacturing process stream waste from a manufacturer of products such as fully cooked tacos, burritos, and taquitos that contained beef. The manufacturing process stream waste contained meat products that had been cooked and offered for human food but that had not been further heat processed for feed. This failure to further heat process the material caused the feed to be adulterated because it contained an unapproved food additive.

Warning Letter Issued for Filthy Animal Feed Warehouse

On June 15, 2004, FDA's Chicago District Office issued a Warning Letter to David W. Bernauer, CEO and Chairman of the Board, Walgreen Co., Deerfield, Illinois. FDA and the Illinois Department of Public Health conducted an inspection of Walgreen's warehouse in Mt. Vernon, Illinois, on February 25 – 27, and on March 2, 2004.

During the inspection investigators documented numerous insanitary conditions which caused the food and drug products stored there to become adulterated. Food and drug products stored and held at the facility were being held in insanitary conditions in violation of the Federal Food, Drug, and Cosmetic Act (the Act).

Evidence of rodent activity was documented throughout the "old" and "new" warehouse which included dead mice in traps, excreta pellets, and gnawed paper material observed in, on, and near food and drugs stored in the warehouse. Rodents gnaw holes were observed in several packaged food products. Many more fecal pellets were on food and drug packages and still more were found near the stored foods, drugs, and cosmetics in the warehouse.

Other conditions observed during the inspection that could be contributing factors to rodent infestation included damaged and/or poorly fitting rail and truck dock doors, gaps around a conduit entry into the building, and the structural condition of the concrete and expansion gaps at floor/wall/support beam junctions in various areas of the warehouse allowing the

entry or harborage of pests. Additionally, the investigators observed cobwebs, dead insects, dust, debris, product spillage, and papers in the warehouse, indicating a general lack of good sanitation practices.

Also, products that contained or may have contained animal protein prohibited ruminant feed failed to bear the caution statement, "Do not feed to cattle or other ruminants." Specifically, pet food products were salvaged, repackaged, and donated without the proper labeling and agreement that they would not be used for ruminants.

Bioresearch Monitoring

University President Issued Warning Letter

Inspections Finds Violations of FDA Regulations Involving INADs

On August 16, 2004, FDA's Center for Veterinary Medicine (CVM) issued a Warning Letter to Edward Richardson, Ed.D., Interim President, Auburn University, Auburn University, Alabama. FDA conducted an inspection of Auburn University between April 7-16, 2004. The inspection was conducted to evaluate the performance of the University as a sponsor of Investigational New Animal Drugs (INADs).

FDA reviewed the inspection report along with the documents collected during the inspection. Based on FDA's evaluation of the information provided in the documents, the Agency concluded that the drug sponsored by the University was unsafe underSection 512 of the Act) and adulterated under Section 501(a)(5), because the University did not operate in accordance with the regulations promulgated pursuant to Section 512(j) of the Federal Food, Drug and Cosmetic Act.

The violations included, but were not limited to the following:

- Failure to assure that the new animal drug was shipped only to investigators who: 1) are qualified by scientific training and/experience to evaluate the safety and/or effectiveness of the new animal drug; 2) maintain complete records of the investigations, including complete records of the receipt and disposition, of each shipment or delivery of the new animal drug under investigation; and 3) furnish adequate and timely reports of the investigation to the sponsor;

- Failure to provide current monitoring; and

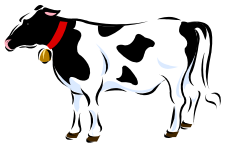
- Failure to submit in triplicate to FDA a "Notice of Claimed Investigational Exemption for a New Animal Drug;" prior to shipment of the new animal drug for clinical tests in animals.

Drug Residues In Edible Animal Tissue

In Fiscal Year 2004, FDA issued over 100 Warning Letters for “Illegal Drug Residues in Edible Animal Tissue.” The following letters are just a few examples of these Warning Letters.

Warning Letter Issued for Penicillin Residue

Sample Analysis Finds .28 Parts Per Million (ppm) in Edible Tissues



On November 25, 2003, FDA’s San Francisco District Office issued a Warning Letter to Mr. and Mrs. Henry A. Vander Poel, Co-Owners, and John C. Vander Poel, Co-Owner, of Whiteside Dairy, Wasco, California. FDA conducted an investigation of this dairy operation in Wasco, California, on September 23 and 26, 2003. The inspection revealed that the firm offered an animal for sale for slaughter as food in violation of the Act.

FDA advised the co-owners that on or about September 2, 2003, the firm consigned a cow to be slaughtered for human food. USDA’s analysis of tissue samples collected from that animal identified the presence of 0.28 parts per million (ppm) penicillin in the kidney. This level exceeds the 0.05 ppm tolerance that has been established for residues of penicillin in cattle kidney. The presence of penicillin at this level in edible tissues from this animal caused the food to be adulterated.

The Warning Letter noted that a food is adulterated under Section 402(a)(4) of the Act if it has been prepared, packed, or held under insanitary conditions whereby it may have been rendered injurious to health. As it applies in this case, insanitary conditions meant that they held animals which were ultimately offered for sale for slaughter as food under conditions which were so inadequate that medicated animals bearing possibly harmful drug residues were likely to enter the food supply.

During the inspection the FDA investigator observed the following:

- Failure to maintain an adequate system for assuring that drugs are used in a manner consistent with the directions contained in their labeling or in a written prescription from the veterinarian;
- Failure to observe the proper withdrawal time for slaughter after treating an animal with a drug; and
- Failure to maintain a drug inventory/accountability system.

Warning Letter Issued for Illegal Residue (Sulfadimethoxine)

On October 30, 2003, FDA's Minneapolis District issued a Warning Letter to Kenneth L. Collier, D.V.M., Co-owner of Friendship Valley, LLC, Clintonville, Wisconsin. FDA investigators conducted an investigation on August 20 and 21, 2003, into an illegal tissue residue in a dairy cow sold for slaughter as human food by Friendship Valley, LLC. The investigation revealed serious deviations from the regulations for Extralabel Drug Use in Animals (21 CFR 530). These deviations caused an animal drug to be used in a manner that was unsafe under Section 512(a) of the Act) and adulterated under Section 501(a)(5) of the Act.

On or about February 18, 2003, Friendship Valley, LLC offered a dairy cow for slaughter as human food. USDA's analysis of tissue samples collected from this cow identified the presence of sulfadimethoxine at 0.32 ppm in the liver and 0.34 ppm in muscle tissue. A tolerance of 0.1 ppm has been established for residues of sulfadimethoxine in uncooked edible tissues of cattle.

FDA's investigation found that the firm failed to comply with 21 CFR 530, because it failed to establish a substantially extended withdrawal period, supported by appropriate scientific information, before marketing of milk or meat prior to prescribing or dispensing an approved animal drug (sulfadimethoxine) for an extralabel use in a food animal. The extralabel use of sulfadimethoxine caused an illegal drug residue in the cow.

Tetracycline Residues Result in Warning Letter

On January 28, 2004, FDA's San Francisco District Office issued a Warning Letter to Larry B. Peterson and Marlene Peterson, Owners of Larry Peterson Dairy, Hilmar, California. FDA received a tissue residue report from USDA reporting the presence of illegal drug residue in

cows that originated from the Larry Peterson Dairy in Hilmar, California.

As a follow-up to USDA's finding, FDA investigators performed an inspection of this dairy operation from November 18 through December 2, 2003. The inspection confirmed that Larry Peterson Dairy was offering animals for sale for slaughter as food in violation of the Act.

On July 11, 2003, the Larry Peterson Dairy sold a dairy cow identified subsequently with USDA retain tag #43071737, for slaughter as human food. USDA's analysis of tissue samples collected from that animal identified the presence of the drug tetracycline in the kidney at 33.06 ppm and in the muscle at 4.47 ppm.

The tolerance level for tetracycline in the kidney of cattle is 12 ppm, and in the muscle of cattle is 2 ppm. The use of tetracycline in this animal resulted in the illegal drug residues found in the kidney and muscle. Therefore, the food was adulterated because it contained a new animal drug that is unsafe.

The Warning Letter advised the firm as it applies in this case, insanitary conditions mean that they hold animals which are ultimately offered for sale for slaughter as food under conditions which are so inadequate that medicated animals bearing possibly harmful drug residues are likely to enter the food supply."

FDA investigators noted the following problems at the dairy:

- Lack of an adequate system for assuring that drugs are used in a manner consistent with the directions contained in their labeling or a veterinarian's prescription labeling. For example, the veterinary label for Tetracycline Soluble Powder prescribes using the drug in a foot bath, to be applied topically once a week, for the prevention of hairy foot warts. The firm did nothing to prevent the cows from drinking (ingesting) the medicated water in the foot bath;

- Lack an adequate inventory/accountability system for determining the quantities of drugs used to medicate the cows and calves; and

- Failure to maintain complete medication treatment records on the dairy cows. For example, the firm's treatment records failed to include the dosage of the drug administered, route of administration for the drug, the person administering the drugs and the withdrawal times for meat and milk.

Consent Decrees of Permanent Injunction Filed Against Four Firms

Anthony DiNitto, Sr., Anthony DiNitto, Jr., and William Nunes

*United States v. Anthony R. DiNitto, Sr., et al.,(*N.D.N.Y.). On October 17, 2003, a Consent Decree of Permanent Injunction was signed in U.S. District Court for the Northern District of New York against Anthony DiNitto, Sr., Anthony DiNitto, Jr., and William Nunes for the sale of cows and calves for human consumption whose tissues exceeded FDA's tolerances for residues of penicillin and sulfadimethoxine.

The use of drugs such as penicillin and sulfadimethoxine in livestock and poultry is strictly regulated by FDA. Before any drug intended for use in animals is approved, it must undergo extensive testing to demonstrate that the food from these animals is safe for human consumption. Withdrawal periods for drugs in edible tissues, which are based upon the depletion and elimination of the drug to a safe residue level in those tissues, ensure that the food we eat is safe and healthful. If an illegal drug residue is detected, FDA investigates the matter and takes regulatory action, if necessary.

A series of violative tissue samples from Anthony DiNitto Dairy were collected from December 31, 1998, through February 15, 2002. DiNitto Dairy produces several million gallons of milk a year. It also ships cull cows (cows that are removed from milking because they are producing too little milk) and calves for human consumption.

Under the terms of the Consent Decree, the defendants must implement systems for identifying animals, record-keeping, drug control, drug accountability, and drug residue withdrawal control.

FDA's New York District Office conducted the investigation that lead to this Consent Decree. FDA's CVM, Office of Compliance, the Office of Chief Counsel, and the U.S. Department of Justice's Office of Consumer Litigation were responsible for the case processing and legal procedures.

Killian Dairy Farm

United States v. Killian Dairy Farm, LLC, (N.D. N.Y.) On July 9, 2004, U.S. District Court Judge Lawrence E. Kahn entered a Consent Decree of Permanent Injunction in this case. The decree perpetually enjoins the defendants from introducing animals or their edible tissues into interstate commerce unless and until the defendants implement to FDA's satisfaction a system of record keeping and procedures to ensure the proper use of new animal drugs and the proper handling of animals to prevent the sale or slaughter of cattle bearing illegal tissue

residues. The defendants were further enjoined from any future violations of the Federal Food, Drug and Cosmetic Act. The Decree provided FDA with the ability to conduct letter shutdown, recall authority, and to apply the arbitrary and capricious standard of review. Defendants have also agreed to pay liquidated damages in the event of noncompliance and for each animal the defendants sell or deliver bearing an illegal tissue residue.

Richard Hayes

Court-Ordered Consent Decree Required Livestock Dealer to Develop Standard Operating Procedures to Prevent Illegal Drug Residues

On May 14, 2004, a Consent Decree of Permanent Injunction was filed in the U.S. District Court for the Northern District of Texas, Amarillo Division, for Richard Hayes of Hereford, Texas, doing business for various livestock companies. Mr. Hayes is a livestock dealer who delivered animals for sale for slaughter as human food. USDA's Food Safety and Inspection Service found that some of these animals had residues of new animal drugs above permitted levels. The drugs included antibiotics such as penicillin, neomycin, gentamicin, tilmicosin, and sulfonamides including sulfadimethoxine and sulfamethazine.

Under the Court-ordered Consent Decree, among other things, Mr. Hayes will develop standard operating procedures to prevent the purchase and sale for human food of animals that have been medicated and not held from slaughter for appropriate amounts of time to deplete potentially hazardous residues; will identify animals; will maintain records of purchase, drug use, and sale; and will train employees.

Dr. Stephen F. Sundlof, Director of FDA's CVM said, “These measures are important as part of an overall residue avoidance program. Identifying and implementing control measures for drug and chemical residues is an important part of FDA's mission of protection of the public health.”

FDA's Dallas District Office conducted the investigation that lead to this Consent Decree. FDA's CVM, Office of Compliance, the Office of Chief Counsel, the U.S. Department of Justice's Office of Consumer Litigation, and the U.S. Attorney's Office in the Northern District of Texas were responsible for processing and filing the case.

Ziegler Dairy Farms, Inc.

On August 10, 2004, a Consent Decree of Permanent Injunction was filed and signed by a Judge in the U.S. District Court for the Western District of Wisconsin, against Ziegler Dairy

Farms, Incorporated, Leo A. Ziegler and Gregory L. Ziegler, as individuals responsible for the operations of the dairy farm. Ziegler Dairy Farms is a family owned dairy farm that raises Holstein dairy cows.

The milk from this farm is sold for human consumption and the farm sells their culled dairy cows for slaughter to produce meat for human consumption. The injunction action is based on 15 illegal tissue residues in edible tissues of eight 8 bovine animals (seven cows and one steer) sampled by the U.S. Department of Agriculture's Food Safety Inspection Service (USDA/FSIS) between March 11, 1998 and March 25, 2003.

The drug residues found by USDA/FSIS included antibiotics such as Lincomycin, Sulfadimethoxine, Gentamicin, Tilmicosin, and Penicillin that were found to be above the permitted tolerance levels or in some cases where no established tolerance for the new animal drug has been established. The Center for Veterinary Medicine is particularly concerned regarding the extra label use of Sulfadimethoxine which is specifically prohibited from extra label use in lactating dairy cows as specified by Title 21 CFR 530.41.

Under the terms of the Consent Decree, the defendants must implement systems for identifying animals, record-keeping, drug control, drug accountability, and drug residue withdrawal control.

Veterinary Drugs

Warning Letter Issued for Serious Violations of CGMPs

On March 31, 2004, the FDA's Kansas District Office issued a Warning Letter to E. Thomas Corcoran, President, Fort Dodge Animal Health, a Division of Wyeth, Inc., Overland Park, Kansas. An FDA inspection on December 1-12, 2003, of this veterinary pharmaceutical manufacturing operation located in Fort Dodge, Iowa, revealed serious deviations from the current Good Manufacturing Practice (CGMP) regulations, Title 21, Code of Federal Regulations, Parts 210 and 211 (21 CFR 210 and 211). Deviations observed during the establishment inspection included, but were not limited to the following:

1. The Quality Assurance Auditing Staff failed to fully follow established Standard Operating Procedure (SOP) 81-003-14 with regard to the auditing of personnel working in the aseptic core. The audits performed did not identify deficiencies in the

systems designed to prevent microbial contamination of drug products purported to be sterile. [21 CFR 211.22(d)]

2. Employees working in the sterile manufacturing area and sterility suite lacked appropriate training in aseptic techniques and aseptic conduct. In addition, these employees failed to follow established SOPS designed to prevent microbiological contamination of drug products purported to be sterile as evidenced by FDA's numerous inspectional observations.

3. The environmental monitoring systems in the small volume parenteral manufacturing and filling areas were deficient in that the firm had not performed a scientific assessment to identify appropriate environmental monitoring sampling sites during the actual manufacturing and sterile filling operations that could pose the most microbiological risk to the products manufactured. Inspectional observations included failure to perform air sampling in the area near the vial turntable to assess the condition of the air during manual loading of vials.

4. No evaluation was performed to show the adequacy and efficacy of the cleaning and disinfection process used in parenteral filling room [redacted] as specified by SOP 14-014-08 [21 CFR 211.42(c)(10)(v)].

5. Investigations of a batch failure or any of its components processed in the aseptic processing area did not extend to other drug products that may have been associated with a specific failure or discrepancy. The heat exchanger used in the Small Volume Parenteral manufacturing rooms [redacted] and [redacted] was found to be contaminating the water for injection (WFI) with bacteria. [21 CFR 211.192 and 21 CFR 211.42(c)(10)(vi)]

6. All established procedures for production and process control for manufacturing of pharmaceuticals were not followed and documented at the time of performance. It is our assessment that the deviations listed above and discussed with your firm's senior management are significant and are a reflection of weaknesses in one or more of the systems designed to control the manufacture of veterinary pharmaceuticals purported to be sterile.

The Warning Letter noted that the firm had revised twenty-two SOPS associated with the sterile core operation, personnel aseptic conduct, environmental monitoring, microbial testing for the water for injection (WFI) system, filter integrity testing, packaging, and product integrity visual examination. Several of the aforementioned SOPS were viewed as critical to achieve cGMP compliance for an aseptic pharmaceutical manufacturing facility.

Warning Letter Issued to Veterinary Health Products Sales Facility

Vet Firm Found Selling Rx Drugs Without a Valid Prescription From a Licensed Veterinarian

On May 20, 2004, FDA's Kansas City District Office issued a Warning Letter to Henry M. Nelson, President, Nelsons Premix Service, Inc., Storm Lake, Iowa. An FDA inspection of this veterinary health products sales facility was conducted on March 2-3, 2004. The inspection revealed that the firm purchased and further distributed prescription drug products for animal use without an order from a licensed veterinarian and without adequate directions for use.

Selling new animal drugs with "adequate directions for use" means adequate directions by which the layman can use a drug safely and for the purposes for which it was intended. Such adequate directions for use by laypersons cannot be written for prescription drugs because the drugs can be used safely only at the direction, and under the supervision of a licensed veterinarian. Dispensing a prescription drug other than by a lawfully written or oral order of a licensed veterinarian resulted in the drug being misbranded.

FDA Issues Warning Letter for Extralabel Drug Use in Animals

On October 27, 2003, FDA's New York District Office issued a Warning Letter to Timothy J. Dennis, D.V.M., Partner, East View Veterinary Clinic P.C., Penn Yen, New York. An FDA investigation of East View Veterinary Clinic and an inspection of a client revealed serious deviations from Extralabel Drug Use In Animals, (21 CFR 530). Such deviations caused the approved animal drug prescribed by Dr. Dennis to be adulterated under Section 501(a)(5) of the Act. The drug was also misbranded under Section 502(t)(1) because its labeling did not bear adequate directions for use.

FDA's regulations require a veterinarian to take certain steps prior to prescribing or dispensing an approved new animal drug for an extralabel use in food animals. Dr. Dennis did not comply with several of these requirements when prescribing and dispensing an approved new animal drug for extralabel use at the dairy farm. Specifically:

- The veterinarian must make a careful diagnosis and evaluation of the conditions for which the drug is to be used (21 CFR 530.20(a)(2)(i)). Dr. Dennis' Patient Medical Record showed that veterinarians from this practice visited the dairy farm a number of times and prescribed and dispensed on four occasions. He was directed to use the drug for the treatment of all classes of adult dairy cattle at his discretion, without

having a veterinarian diagnose and evaluate the conditions for which the drug was to be used.

- The veterinarian must institute procedures to assure that the identity of the treated animal or animals is carefully maintained (21 CFR 530.20(a)(2)(iii)). Specifically, Dr. Dennis stated that he had not instituted procedures to assure that the identity of treated animals are maintained and assigned withholding times have been satisfied.

In addition to the above, a prescription label failed to conform to 21 CFR 530.12 in that the labeling failed to include the class/species or identification of animals being treated, the dosage frequency and duration of treatment, and any appropriate cautionary statements. Such deviations caused the drug to be misbranded.

Veterinary Pharmacy Compounding

Warning Letter Issued to Veterinary Drug Compounding Operation

On November 25, 2003, the FDA's Dallas District Office issued a Warning Letter to Jack R. Munn, R.Ph., President, Medical Park Pharmacy, Dallas, Texas, a veterinary drug compounding operation. An FDA inspection on July 28/August 6, 2003, disclosed significant violations of the Federal Food, Drug, and Cosmetic Act (the Act). The FDA investigator was accompanied by Cy Weich, R.Ph., Chief Compliance Officer of the Texas State Board of Pharmacy (TSBP). This investigation determined that Medical Park Pharmacy was exceeding the regulations under which a compounding pharmacy may compound veterinary drugs.

The Warning Letter noted the use of bulk active pharmaceutical ingredients (APls) under circumstances that create public health concerns. When used in food animals, these drugs present particular safety concerns because of the possibility that unsafe drug residues could occur in edible tissues. The compounded drugs were essentially duplicates of FDA approved animal drug products available on the market. Additionally, some compounded animal drugs, such as cisapride, were withdrawn from the market for human use for safety reasons

The prescription drugs distributed to individuals, farms, ranches, feed stores, veterinarians, and animal clinics by Medical Park Pharmacy often failed to record critical information necessary to establish treatment for a specific species, or identification of the animal(s) to receive treatment. Prescription drug labeling frequently failed to indicate directions for use, and instead indicated "See Veterinary References for Dosage for Species and Organism." Drugs compounded for food animals did not bear a withdrawal time established by a State

licensed veterinarian; instead withdrawal times printed on the firm's product labels were provided by the firm, and were not backed by scientific data supporting the withdrawal periods indicated.

Section 512, in part, deems a new animal drug to be unsafe unless an approved New Animal Drug Application (NADA) is in effect for "the specific product in question." None of the animal drugs Medical Park Pharmacy compounded and distributed are the subject of an approval by FDA.

The only legal compounding of animal drugs is provided under the Animal Medicinal Drug Use Clarification Act and its implementing regulations at 21 CFR Part 530, Extralabel Drug Use in Animals. 21 CFR 530.13 allows a veterinarian or pharmacist to compound animal drugs on the lawful written order of a licensed veterinarian only if certain conditions are met. The conditions include the requirement that the compounding be within the context of a valid veterinanian-client-patient relationship (VCPR), and that the compounding be conducted only with the use of approved drug product. However, Medical Park Pharmacy compounded animal drugs using bulk APIs, which is not permitted under 21 CFR 530.13(a).

Moreover, some of these animal drugs were compounded using the bulk drug substance cisapride, which was withdrawn from the market for safety reasons. In addition, it appeared that Medical Park Pharmacy's products were being compounded outside the context of a valid VCPR, as required by 21 CFR 530.10(a), and that the products were not labeled with directions for use specified by a veterinarian, including the animal or animals in which the drug is intended to be used.

Warning Letter Issued to Veterinary Pharmacy for Illegal Drug Compounding

On October 6, 2003, the FDA's Dallas District Office issued a Warning Letter to Dr. Warren B. Lee, President, Lee Pharmacy, Inc., Fort Smith, Arkansas. FDA conducted an inspection of Lee Pharmacy on December 11/13, 2002. The inspection was conducted pursuant to the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. 321 et, seq., as authorized by Inspection Warrant No. FS-02-38, signed by United States Magistrate Judge Beverly Stites Jones, and filed on December 10, 2002, in the United States District Court for the Western District of Arkansas, Fort Smith Division. The inspection disclosed serious violations of the Act.

The Warning Letter noted that FDA was in receipt of the firm's post inspection written correspondence dated December 24 and 26, 2002, and January 8 and 24, and February 21, 2003. The Agency acknowledged the changes that the firm indicated were being made to their compounded human drug products. However, the Warning Letter noted that the Agency found that the firm's response regarding veterinary drugs to be unsatisfactory, because Lee

Pharmacy made no statements indicating that the corrective actions would ensure that prescription veterinary drugs would not be compounded with the use of bulk active pharmaceutical ingredients (APIs).

Compounded Veterinary Drug Products:

Lee Pharmacy compounds veterinary prescription injectable drug products, which are shipped to veterinary clinics for use in large and small animals, including food producing animals. The veterinary drugs compounded and distributed by the firm are adulterated under Section 501(a)(5) of the Act because they are unsafe within the meaning of Section 512 of the Federal Food, Drug and Cosmetic Act. Under Section 512, a new animal drug is deemed unsafe unless an approved New Animal Drug Application (NADA) is in effect for the specific product in question. None of the animal drugs compounded and distributed by the firm are the subject of an approved NADA.

The only legal compounding of animal drugs is provided under the Animal Medicinal Drug Use Clarification Act and its implementing regulations at 21 CFR Part 530, Extralabel Drug Use in Animals. FDA's investigation found that Lee Pharmacy did not comply with these requirements. For example, 21 CFR 530.13(a) requires that the compounding be conducted using approved animal or human drug products. However, the firm compounded with the use of bulk active pharmaceuticals ingredients, which is not permitted.

Moreover, some of the veterinary products were compounded with the use of bulk drug substances, such as camphorated oil and cisapride, that have been withdrawn or removed from the market for human use for safety reasons. In addition, it appeared the products were being compounded outside the context of a valid veterinarian-client-patient relationship, as required by 21 CFR 530.10(a), and that the scale of the firm's compounding operation was not commensurate with the established need for the compounded products, as required by 21 CFR 530.13(b)(5).

Seizure of Illegal Compounded Veterinary Drugs

At the request of FDA, the U.S. District Court for the Eastern District of Kentucky issued a seizure warrant on August 11, 2004, for various illegally compounded drug products for use in horses found at BET Pharm, LLC, Lexington, Kentucky. The U.S. Marshals Service executed the seizure warrant on August 12, 2004.

FDA's inspections of BET Pharm, LLC, revealed the firm is illegally manufacturing and

distributing unapproved animal drugs intended for various uses in horses. These drug products and their components were subject to seizure by the federal government because the drug products were not approved by FDA as new animal drugs and thus were adulterated under the Federal Food, Drug and Cosmetic Act.

BET Pharm, LLC, was previously issued a Warning Letter outlining unacceptable practices. The Warning Letter cited violations including manufacturing drug products from bulk drugs without approval from FDA, compounding of drug products that are copies of approved drugs, and selling compounded drugs in the absence of a valid relationship between a veterinarian and horse owner. The company was given an opportunity to correct the violations, but failed to take appropriate actions.

The articles are intended for various uses in horses, including to induce ovulation and help maintain pregnancy, and to treat Cushing's disease.

The articles of veterinary drug compounded and distributed by BET Pharm, LLC, are adulterated because they are new animal drugs in that they are not generally recognized by qualified experts as safe and effective for their intended uses, and they were therefore unsafe. A new animal drug is deemed to be unsafe unless an approved new animal drug application (NADA) is in effect for the specific product and use in question. None of the animal drugs compounded and distributed by BET Pharm, LLC, were the subject of an approved NADA.

All of the articles are misbranded because their labeling fails to bear adequate directions for use and they are not exempt from this requirement because they were unapproved new animal drugs.

FDA issued a Warning Letter to BET Pharm, LLC, in November 2003, following an inspection conducted in June-August 2003. The letter advised the firm that its compounding practices were in violation of the Act and that the compounded products were adulterated because they were new animal drugs compounded from bulk drugs, which is not permitted by 21 CFR 530.13(a), and that the products were also misbranded.

The letter stated that failure to correct the violations may result in regulatory action, including seizure or injunction, without further notice. In December 2003, the firm's attorney replied, disagreeing with FDA's position and stating that the firm's practices were in compliance with the law. A subsequent FDA inspection on May 6-18, 2004, disclosed that the firm continued to operate in the same fashion with the same violations of 21 U.S.C. 351(a)(5) and 352(f)(1).

Pharmacies are not exempt from the approval requirements in the new animal drug provisions of the Act. Animal drug compounding allowed under the Act is limited to the preparation of drug products that do not meet the definition of new animal drugs. In the absence of an approved NADA, the compounding of a new animal drug from any bulk drug results in an adulterated new animal drug.

Two federal appellate decisions, United States v. Algona Chemical Inc., 879 F.2d 1154 (3d Cir. 1989), and United States v. 9/1 Kg. containers, 854 F.2d 173 (7th Cir. 1988), affirmed FDA's position that the Act does not permit compounding of unapproved finished drug products. Although these cases predate the Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA) amendments, the principle established by these cases remains fully viable today with regard to the manner in which this firm operates.

AMDUCA, 21 U.S.C. 360b(a)(4), explicitly allows some extra-label drug use of approved drugs and implicitly allows compounding for such use provided that approved new drugs are used for such compounding. These amendments specifically apply only to approved new animal drugs. See also, 21 CFR 530.13(a) (prohibiting, inter alias, compounding from bulk drugs).

These violations could pose a health risk to horses because the safety and efficacy of these drugs are not known. FDA advises horse owners not to purchase or use these products. Horse owners may wish to consult their veterinarians for advice on which products are appropriate to treat their animals.

FDA initiated this action as part of its responsibility to promote and protect the health of animals by enforcing the animal drug, device, and feed provisions of the Act. FDA's mission includes ensuring the safety or safety and effectiveness of a broad spectrum of regulated animal products, including feed, drugs, and veterinary devices.